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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/715,810	11/17/2003	Shengwen Li	ALLE0004-100 (17614(BOT))	5198

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 02/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/715,810	LI ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-72 is/are pending in the application.

4a) Of the above claim(s) 3,4,12-17 and 22-72 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1,2,5-11 and 18-21 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 11/17/03 &5/12/04 is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 4/12/04.
4) ☑ Interview Summary (PTO-413) Paper No(s)/Mail Date. 12/1/04
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A preliminary amendment filed May 12, 2004 is acknowledged, where the original Figs. 1 and 2 were substituted.

Election/Restrictions

2. Applicant's election with traverse of Group I, claims 1, 2, 5-11 and 18-21 during a telephone conversation with Quan Nguyen on December 14, 2004. Claims 3, 4, 12-17 and 22-72 are non-elected inventions and are withdrawn from consideration. Thus, claims 1, 2, 5-11 and 18-21 are examined.

Informalities

The disclosure is objected to because of the following informalities:

3. Fig. 2 is objected to because the drawing recites the peptide sequence of SEQ ID NO:5 being SEQ ID NO:39, which is not correct. Appropriate correction is required.

4. The specification recites amino acid and nucleotide sequences at pages 25 (e.g., tetrapeptides), 26, 37 and 38, however, there are no sequence identifiers "SEQ ID NO:" provided. Applicants must comply with the requirements of the sequence rules (37 CFR 1.821-1.825) and provide a new copy of sequence listing and CRF containing all the sequences.

Claim Rejections-Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1, 2, 20 and 21 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 10 of U. S. Patent 6,203,794. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1, 2, 20 and 21 in the instant application disclose a method of treating a botulinum toxin intoxication in a mammal by administering an effective amount of a rescue agent such as the rescue agent comprising an inactive botulinum toxin. This is obvious in view of claim 10 in the patent which disclose a method for treating a mammal having acute botulinum poisoning comprising administering an effective amount of a solution comprising an inactive clostridial neurotoxin having an inactivated light chain and an unaltered heavy chain, and a drug joined to the inactive light chain of the inactive neurotoxin. The claims of the instant application and the claim of the patent are directed to a method of treating a botulinum toxin intoxication in a mammal by administering an effective amount of a rescue agent comprising an inactive botulinum toxin. Thus, claims 1, 2, 20 and 21 in present application and claim 10 in the patent are obvious variations of a method of treating a botulinum toxin intoxication in a mammal by administering an effective amount of a rescue agent comprising an inactive botulinum toxin.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 2, 6-11 and 18-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 2, 6-11 and 18-21 are directed to a method of treating a botulinum toxin intoxication in a mammal by administering an effective amount of a rescue agent such as the rescue agent comprising an inactive botulinum toxin. While the specification indicates the present invention provides for effective methods of treating botulinum intoxication comprising administering an effective amount of a rescue agent, where a rescue agent comprises at least one of inactive botulinum toxin (iBoNT), for example, a glycosylated iBoNT, which has a reduced antigenicity (paragraph [0027]), the specification does not disclose a genus of variants for a rescue agent or an inactive botulinum toxin in the method of treating a botulinum toxin intoxication in a mammal.

The specification indicates that a rescue agent comprises an iBoNT, which contains a heavy chain and a light chain, wherein the light chain is mutated as to have minimal or no ability to interfere with the release of neurotransmitters from a cell or a nerve end, e.g., iBoNT/A having the amino acid sequence of SEQ ID NO:4 (paragraph [0060]); the iBoNT, which is glycosylated, has reduced or no antigenicity (paragraphs [0061]-[00102]); and the use of g-iBoNT as antidote in accidental overdose in the treatment of postherpetic neuralgia (Example 8), or for detoxification (Example 9). However, the specification does not describe a genus of variants for

a rescue agent or an inactive botulinum toxin in the method of treating a botulinum toxin intoxication in a mammal. A single species of a rescue agent (e.g., iBoNT/A having the amino acid sequence of SEQ ID NO:4 (iBoNT/A-Hall (H227Y); Fig. 10) or the glycosylated thereof) do not provide original descriptive support for a genus of variants for a rescue agent or an inactive botulinum toxin. The variants of rescue agents do not meet the written description provision of 35 USC 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

Applicants have described a specific inactive botulinum toxin (iBoNT/A-Hall (H227Y); Fig. 10) in the method of treating a botulinum toxin intoxication in a mammal, however, a genus of variants for a rescue agent or an inactive botulinum toxin have not been sufficiently described.

The skilled artisan cannot envision all the contemplated compounds based upon the general suggestion of a functional characteristic of a rescue agent or inactive botulinum toxin in the claimed method. The detailed structures must be taught, therefore conception cannot be not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of preparation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of making. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30

USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF'S were found unpatentable due to lack of written description for the broad class.

Therefore, only those embodiments described and disclosed meet the written description requirement and not the full breadth of the claim meets the written description provision of 35 USC 1 12, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 2, 5-11 and 18-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2, 5-11 and 18-21 are indefinite as to what effective amount of at least one rescue agent would do in the method treating a botulinum toxin intoxication. Claims 2,.5-11 and 18-21 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1, 2, 20 and 21 are rejected under 35 U.S.C. 102(b) as anticipated by Dolly *et al.* (U.S. Patent 6,203,794, publication date: March 20, 2001).

Dolly *et al.* teach the use of an inactive clostridial neurotoxin in the preparation of a medicament for treating botulinum toxin poisoning, wherein the inactive clostridial neurotoxin (e.g., botulinum toxin A modified at His^{227} (to Tyr^{227}) or Glu^{224} (to Gln^{224})) can be used either alone or conjugation to another drug (e.g., Captopril or another zinc protease inhibitor), and wherein a therapeutically effective amount of the conjugate or inactive toxin is administered by intramuscular injection (column 2, lines 13-56; Example 18; column 36, lines 1-26; claims 1, 2, 20 and 21).

9. Claims 1, 20 and 21 are rejected under 35 U.S.C. 102(b) as anticipated by Lisk *et al.* (WO 2002/089834, publication date: November 14, 2002).

Lisk *et al.* teach a method of treating a patient with botulinum toxin A (BoNT/A) or botulinum toxin C1 (BoNT/C1) poisoning by administering botulinum toxin E (BoNT/E) or a fragment of synaptosomal-associated polypeptide of 25 kDa (SNAP-25) obtained by the cleavage of SNAP-25 with BoNT/E, wherein the toxin is administered by intramuscular injection (page 5, line 24-page 6, line 15; Example 1; page 18, line 13-page 19, line 5; page 33, lines 14-24; claims 1, 20 and 21).

Conclusion

10. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Patent Examiner

CMK
February 16, 2005